

ORIGINAL ARTICLE

Intermediate-term Outcome of Psychiatric Inpatients with Major Depression

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Background/Purpose: A wide range of recovery rates has been reported during the 1st year of follow-up in patients with depression, and there is a lack of consensus regarding which clinical and psychosocial variables are associated with prognosis. This study investigated the outcome of inpatients with a major depressive episode at 10–22 months (mean \pm SD = 14.0 \pm 3.4 months) of follow-up and the associated psychosocial and clinical variables.

Methods: The demographic and clinical characteristics of 67 inpatients with a DSM-IV major depressive episode were assessed at admission, discharge and 1 year after the initial assessment. A logistic regression model was used to examine the predictive factors of depressive status at follow-up.

Results: At the 1-year follow-up, 12 patients could not be located, one refused further interview and one had committed suicide 1 month after discharge. Eighty percent of patients had follow-up examinations. Out of 67 patients, 31 (47%) underwent a DSM-IV diagnosis (29 with major depression and two with minor depression) and 22 (33%) recovered. Low socioeconomic status ($p=0.05$), long duration of illness before admission ($p=0.03$) and number of previous hospitalizations ($p=0.04$) were predictive factors for a depressive morbidity at 10–22 months.

Conclusion: At follow-up, almost half of the discharged depressive patients were still depressed. Screening for predictive factors of chronic depressive morbidity facilitates better outcome by considering the heterogeneity of psychopathology that can lead to failure in the treatment plan. [*J Formos Med Assoc* 2006;105(8):645–652]

Key Words: inpatient, major depression, outcome, predictive factors

Depression is now considered to be the world's fourth greatest public health problem.¹ A great deal of evidence on the outcome and course of this disorder shows that depression is a chronic and recurrent disorder in contrast to Krepalin's earlier concept.^{2–5} Chronic depression develops in more than 20% of patients after an index episode. Partial recovery will occur in 15–20% of patients and 15–35% of patients who recover will relapse within 1–2 years.^{2,6–9} The estimated probability of remaining ill for at least 5 years

was 11.5%.³ Among those who were not well for the first 5 years, 38% recovered within the next 5 years.¹ Only a quarter of patients recovered from an index episode and remained well for more than 10 years thereafter. For more than one in 10 patients, depression proved to be persistent; the proportion of patients affected remained relatively stable over time.¹⁰

Review of a limited number of naturalistic outcome studies of affective disorders in which depression was followed up for approximately

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1 year showed a wide range of recovery rates from depression (35–75%).¹⁰ There is also no consensus regarding which clinical and psychosocial variables are associated with prognosis. Several methodologic considerations hamper comparison of the results from the few available naturalistic studies. Follow-up studies of patients with depressive disorders varied widely in definitions of recovery and follow-up period (determined from the starting point since disease onset, enrollment into a study or discontinuation of inpatient treatment), in methods of study design (prospective and periodic assessments with short intervals or assessment at an end point) and outcome assessments (depression defined by an interview method or by questionnaires), as well as in composition of subjects from the community, outpatients or inpatients.

This study aims to investigate the outcome status of depressive inpatients at 10–22 months' follow-up and the effects of psychosocial and clinical variables (including inpatient treatment) on intermediate-term clinical outcome after discharge.

Methods

Subjects

Sixty-seven patients with a current episode of DSM-IV major depressive disorder (MDD) without psychotic features who were consecutively admitted to a psychosomatic ward of a university hospital from October 2000 to June 2001 were included. None of these patients had a previous episode of hypomania or mania. Three patients had repeated hospitalization during the study period and therefore received study assessment only once. These subjects were originally recruited as a pretest group of outcome in a clinical pathway for depressive inpatients.

Measurements

Data recorded for each patient included age at onset of depression, number of previous hospitalizations, duration of illness before index admission, family history of psychiatric illness, the presence of coexisting disorders, concomitant

suicide attempt and length of hospital stay. Socio-economic status (SES) was stratified into quintile categories, classes I–V, ordered from highest to lowest and based on education and occupation of key person in their family.¹¹

The Hamilton Rating Scale for Depression (HAM-D) and the Beck Depression Inventory (BDI) were used to assess the severity of depression as well as the treatment response of depression.^{12,13} Response to treatment was defined as a HAM-D score at discharge that had decreased by more than 50% from baseline, and remission of depression as a HAM-D score ≤ 7 .¹⁴ A recent study comparing the reliability and validity of face-to-face and phone interviews for HAM-D found high levels of agreement (Pearson's correlation coefficient $r = 0.748$).¹⁵

The Global Assessment of Functioning (GAF) scale was used to provide a clinician's assessment of a patient's overall level of functioning on a hypothetical continuum of mental health illness.

The Maudsley Personality Inventory (MPI) by Eysenck measures two aspects of personality characteristics: neuroticism and extroversion.¹⁶ Its psychometric properties and time stability have been demonstrated, and it has been widely used in both community and medical settings in Taiwan since the 1970s.^{17,18}

The Family APGAR index, developed by Smilkstein in 1978, is a family function-screening questionnaire, which measures the perception of five components of family function: adaptation, partnership, growth, affection and resolve.^{19,20} A higher score indicates a higher level of family support.

The Mini International Neuropsychiatric Interview (MINI) is a short structured diagnostic interview, developed jointly by psychiatrists and clinicians in the United States and Europe, for DSM-IV and ICD-10 psychiatric disorder.²¹ In 1999, after obtaining a permission agreement from the original authors, MINI was translated into Chinese by a two-step procedure (translation and back-translation) in Taiwan. A research and development team was organized, and senior psychiatrists working in medical centers and

psychiatric institutes were invited to discuss and examine the content validity of the Taiwanese version of the MINI on several occasions. A psychiatrist experienced with the use of this instrument was also invited to attend the training workshop conducted by the Taiwanese Society of Psychiatry in Taipei, and MINI training was held annually and integrated into the resident training programs in our department.

Procedure

Acute phase: During the 1st week of hospitalization, attending psychiatrists rated the severity of depression and functioning level of the hospitalized patients with the HAM-D-17 and GAF scales. Patients were also asked to complete the BDI, MPI and Family APGAR. Three days before discharge, these assessments were repeated except for the MPI and Family APGAR.

Follow-up: Follow-up was conducted beginning at approximately 1 year after patients were discharged from hospital. The mean duration of follow-up (from the time of discharge to the time at follow-up) was 14.0 ± 3.4 (10–22) months. One of the authors collected data on sociodemographic and clinical characteristics during the index admission using the chart review method.

Sixty-seven patients were contacted by telephone or by mail according to their previously known addresses. The purpose of the initial contact included addressing the aim of this study and invitation for a follow-up interview after obtaining written consent. The follow-up interview was conducted over the telephone if patients were not available for face-to-face interview at the hospital. Follow-up assessments comprised two parts: patients' interviews and self-report questionnaire (BDI). A senior psychiatrist conducted a structured diagnostic interview (MINI) to establish each patient's diagnostic status and HAM-D and GAF evaluation at follow-up.

This study was naturalistic by design. Information was collected on treatments received in hospital and after discharge, but no attempt was made to control the amount or type of therapy given to patients.

Statistical analyses

Descriptive statistics were used to analyze basic demographic data. For the purpose of comparison, the denominator of rates of follow-up in this study as well as other comparative studies included all originally recruited patients. Paired *t* test was used to compare the psychometric scores (HAM-D, BDI and GAF) between admission and discharge. In the analysis, the depression outcome variable was dichotomized into case group or recovery group. Recovery from a depressive episode was defined as absence of DSM-IV depressive disorders for at least 8 weeks according to status at 1-year follow-up after discharge from hospital. Differences in variables between the two groups were compared with *t* or χ^2 tests for continuous or categorical variables, respectively. All the sociodemographic and clinical variables (included psychometric scores) were examined for relationship with outcome of depression at follow-up. If a significant bivariate relationship was found, the factor was included in a multivariate logistic regression model to determine if it was an independent predictor of depressive status at follow-up. All data were analyzed using SPSS version 10.0 (SPSS Inc., Chicago, IL, USA) for Windows.

Results

Basic and clinical characteristics

Most of the patients were women ($n = 48$, 71.9%), and the mean age of the patients at admission was 49.2 ± 15.4 years. Thirty-one percent and 42% of the patients were in upper or middle SES categories, respectively. The mean duration of the index episode of MDD prior to study entrance was 6.0 ± 8.7 months, with nearly 60% of them less than 3 months. The index episode was the patient's first episode for 40% of all patients, and 24% had at least two prior episodes.

Treatment response and clinical status at discharge

All patients received an equivalent dosage of 178.7 ± 64.7 mg imipramine or 35.7 ± 12.9 mg

fluoxetine during hospitalization.²² After an average of 25 days of hospitalization, 79% ($n=53$) of all patients responded to treatment (defined by HAM-D score $<50\%$ of original score), and 60% ($n=40$) achieved remission (HAM-D ≤ 7) at discharge. Psychometric scores including HAM-D (22.4 *vs.* 7.7, $t=17.0$, $p<0.001$), BDI (31.9 *vs.* 20.9, $t=6.6$, $p<0.001$) and GAF (45.5 *vs.* 69.8, $t=-14.6$, $p<0.001$) were significantly improved at discharge compared with at admission.

Attrition

At follow-up, 12 patients could not be located, one refused interview and one had committed suicide by jumping from a building 1 month after discharge. Among the patients successfully contacted, 53 completed the study yielding a participation rate of 80.3% (excluding the 1 patient who died). Forty-seven patients (88.7%) were interviewed face-to-face, and the remaining (11.3%) were interviewed by telephone. No significant differences in demographic or clinical variables were found between patients who dropped out and those who completed the study. Most of the attrition cases (85.7%) were in a state of remission at discharge.

Outcome status at follow-up

Good drug compliance during the follow-up period was reported by about 80% of patients. The equivalent dose was 131.9 ± 78.1 mg imipramine or 26.4 ± 15.6 mg fluoxetine. Forty-seven percent of 67 patients ($n=31$) met the criteria for DSM-IV depressive disorders at follow-up and were labeled as the case group. Among them, 93.5% ($n=29$) met the criteria for MDD and 6.5% ($n=2$) for minor depressive disorder. Thirty-three percent ($n=22$) of patients had no or minimal symptoms of depression for at least 8 weeks at follow-up and were designated as the recovery group. Among them, only one-quarter of 67 patients ($n=17$, 25.4%) had recovered from the index episode and remained well during the follow-up period. The HAM-D scores for the two groups at follow-up were 18.4 ± 6.9

and 4.4 ± 3.8 , respectively. The BDI scores were 29.5 ± 8.8 and 7.6 ± 9.7 , respectively. The outcome for the 20% of this sample that was lost during follow-up or declined follow-up examinations was unknown.

Predictive factors for depression outcome at 10–22 months of follow-up

Clinical and sociodemographic factors significantly related to depressive illness at follow-up included SES ($p=0.01$), suicide attempt at index episode ($p=0.05$), number of previous hospitalizations ($p=0.03$) and longer duration of illness before index admission ($p=0.04$) (Table 1). There were no significant differences in outcome status at around 1 year based on patients' sex, age, marital status, age at onset of depression, family history of psychiatric illness, presence of comorbid physical illness, treatment modality (combination of antipsychotics or electroconvulsive therapy), length of hospital stay, severity of symptoms (BDI, HAM-D and GAF scores) at index admission, neuroticism scores of MPI, Family APGAR, remission status at discharge or compliance at outpatient follow-up. The best model to predict depressive illness at follow-up showed that lower SES, longer duration of illness before entry, more frequent previous hospitalizations and suicide attempt at index episode were significant risk factors (Table 2). The final adjusted model correctly identified 81.1% of the cases.

Discussion

Comparison of our results with those of Keitner et al²³ showed that our patients had a similar rate of depression at follow-up (47% *vs.* 46%), a lower rate of recovery (33% *vs.* 44%) and a higher attrition rate (20% *vs.* 10%). Previous studies which used different methods to examine the recovery rate found a higher percentage of patients recovered including 62% in Sargeant et al's study,²⁴ 54.2% in Ezquiaga et al's study²⁵ and 74% in Keller and Shapiro's 1-year follow-up results.⁸ Sargeant et al adopted the presence or absence of major

Table 1. Comparison of characteristics of patients with depression and recovery at 1-year follow-up

	Depression at follow-up (n = 31)	Recovered at follow-up (n = 22)
Sex, female (%)	71.0	68.2
Marital status (%)	25.8	36.4
SES, I & II (%) [*]	19.4	59.1
Mean age (yr)	50.1	51.6
Mean age at onset (yr)	45.3	46.3
Family history of psychiatric illness (%)	12.9	18.2
Comorbidity with physical illness (%)	35.5	50.0
Previous hospitalization (n) [†]	1.0	0.2
Previous hospitalization ≥ 2 (%) [†]	19.4	0
Suicide attempt at index episode (%) [†]	38.7	13.6
Mean duration of index episode (mo) [†]	8.9	3.9
Length of stay (d)	26.7	26.0
Treatment		
With antipsychotic (%)	22.6	18.2
With ECT (%)	9.7	0
Remission status at discharge (%)	58.5	45.5
Psychometric scores at admission (mean ± SD)		
BDI	32.5 ± 11.1	30.0 ± 12.6
HAM-D	21.9 ± 7.7	23.5 ± 7.4
GAF	44.4 ± 10.1	44.8 ± 9.5
Neuroticism of MPI	15.6 ± 5.4	14.6 ± 3.9
Family APGAR	5.8 ± 4.3	5.9 ± 4.2

^{*}*p* < 0.01; [†]*p* < 0.05. SES=socioeconomic status; ECT=electroconvulsive therapy; BDI=Beck Depression Inventory; HAM-D=Hamilton Rating Scale for Depression; GAF=Global Assessment of Functioning; MPI=Maudsley Personality Inventory.

Table 2. Logistic regression analysis of risk factors with depression outcome at follow-up

Risk factors	β	SE	<i>p</i>	OR	95% CI for OR	
					Lower	Upper
SES [*]	0.96	0.50	0.05	2.61	0.98	6.89
Duration of illness before entry (d) [†]	0.16	0.71	0.03	1.17	1.02	1.35
Number of previous hospitalizations	1.42	0.68	0.04	4.14	1.10	15.55
Suicide attempt at index admission	1.35	0.83	0.10	3.87	0.76	19.75

Note: A multiplier greater than 1 indicates an increased likelihood of depression persistence at follow-up.

^{*}Lower SES increased the odds of being depressed at follow-up (1=upper SES, 2=middle SES, 3=lower SES); [†]longer duration of illness significantly increased the odds of being depressed at follow-up. CI=confidence interval; OR=odds ratio; SES=socioeconomic status.

depression after 1 year as the outcome variable in a community population. Ezquiaga et al followed up 72 outpatients suffering from a unipolar major depression, using a prospective, periodic assessment of HAM-D and other psychosocial variables. The lower rate of persistent depression perhaps reflected the presence of less

severe illnesses in the community and outpatient group. Keller et al's study defined rates of recovery and subsequent relapse in terms of the percentage recovered and/or relapsed at any time up to 1 year rather than in terms of how well patients were at the time of follow-up. The inclusion of some outpatients is another possible explanation

for why Keller et al's patients had better outcome. In agreement with Keller et al's results (30%), our study found that only 25.4% of patients had recovered from the index episode and remained symptom free for the remainder of the 1-year follow-up period.

In this study, the only demographic factor predictive of depression at 1 year was sociodemographic status. The effects of age, sex and marital status on the course and outcome of depression were not confirmed in many follow-up studies, as well as in this study. In previous studies, SES was not consistently implied to have a relationship with persistence of depression. Low family income or low level of education was found to be a predictor of chronicity in two previous studies.^{7,26} Another meta-analysis regarding the relationship of SES and depression indicated that individuals with low SES had higher odds of being depressed (odds ratio [OR], 1.81).²⁷ Once depressed, individuals with lower SES were much more likely to have persistent depression (OR, 2.06).

Only two clinical variables, longer duration of illness and more frequent hospitalizations, were associated with persistence of depression at follow-up in this study. The significance of suicide attempts disappeared after adding number of previous hospitalizations as a variable in the logistic regression model. Several previous studies of community- and patient-based samples have demonstrated the relationship between duration of illness and depressive outcome.^{7,8,24,28–30} The number of previous hospitalizations was also related to depressive outcome in two studies.^{8,23} Patients who had suffered from index depressive episode for a longer time before admission or had more previous hospitalizations were at a higher risk of a chronic disease course. This result highlights the need for depressed patients to receive early inpatient treatment. However, decisions for hospitalization should be adequately considered based on the benefit of early admission to prevent chronicity of depression and the cost of repeated hospitalizations that reinforce chronicity.

Severity at presentation,²⁴ length of stay,²³ age at onset,²³ social support^{26,31} and remission from

depression with residual symptoms³² have been described as predictors of persistent depression in previous follow-up studies. A high level of neuroticism was reported to be associated with a slower time to recovery.^{33,34} None of the above factors was confirmed as an outcome predictor in this study. An inadequate treatment regimen was assumed to be responsible for the unfavorable outcome of depressive episodes in patients with personality pathology.^{26,35} Our patients received an adequate dosage and duration of antidepressants as well as psychosocial treatment during hospitalization and follow-up. Remission status was defined according to assessments performed at discharge (when clinical conditions reached steady progress or chronic stable) instead of at regular time intervals after starting treatment. The above two reasons might explain why no significant relationship was found between some factors (high level of neuroticism, severity of presentation and remission status at discharge) and persistent depression in this study.

This study had several limitations. First, the study design was naturalistic, i.e., treatment was not assigned by design but left to the discretion of the patients. Therefore, assessment of the effect of treatment in this study is problematic. Second, researchers assessed patients' clinical status only at admission, discharge and 10–22 months later. Data collected from the patients regarding the clinical course might be biased by patients' recall. Recovery followed by relapse or recurrence at the time of follow-up would lead to underestimation of the recovery rate. Third, the resulting bias toward underestimating outcome was confounded by lack of follow-up in some subjects. In conclusion, at 1-year follow-up, nearly half of the discharged depressive patients were still depressed; only one-quarter of them had sustained recovery throughout the follow-up period. Lower SES, longer duration of illness before admission and greater number of previous hospitalizations were risk factors associated with lack of recovery at 1 year after a depressive episode in order of significance. For patients with a discrete episode of depression, early admission

to shorten the duration of the current episode might provide an alternative treatment modality to lessen the risk of continued depression at follow-up. However, for patients with chronic depressive symptoms and poor response to previous treatment, the benefit of inpatient therapy should be balanced against the cost of repeated hospitalizations that might also enhance the chronicity of depression itself. Screening for risk factors of continued depression facilitates optimal treatment based on the heterogeneity of psychopathology.

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